

REMARKS**I. INTRODUCTION**

Receipt of the Office Action of December 2, 2002 is acknowledged. Applicants appreciate the indication that claims 10 and 11 are free of the prior art. Claim 23 has been canceled without prejudice or disclaimer. The chemical substances encompassed by claim 23 are directed to non-elected species. Claims 1, 4 and 5 have been amended in the present response. Claim 1 has been amended to recite the subject matter that the Examiner has considered, i.e., R⁹ is alkyl substituted with substituted or unsubstituted nitrogen. Claims 4 and 5 have been amended to correct an obvious typographical error, substituting NR¹¹R¹² for the recitation in the claims of R¹¹R¹².

Upon entry of the amendments to the claims, claims 1-5, 9-16 and 18-22 and 24 will be pending in this application.

II. THE OFFICE ACTION**Restriction/Election**

The Examiner has maintained the restriction between compounds and composition claims and method of use type claims. It is respectfully pointed out that according to In re Ochiai, the PTO is required to rejoin method of use claims which are of the same scope as product claims upon a finding that the product claims are allowable. As stated in the reply to the Restriction Requirement filed September 26, 2002, "It is respectfully submitted that pursuant to the *Official Gazette* notice of March 26, 1996 which establishes guidelines for treatment of product and process claims in light of In re Ochiai, claims 13, 14 and 16-22 should be included herein for consideration on the merits." Furthermore, the Examiner states that "the process for using the product as claimed can be practiced with another materially different product." It is respectfully pointed out that the method of use claims are directed to therapeutic methods of use wherein the compound administered is a compound of claim 1. Thus, while another compound having activity as a protein kinase inhibitor may be useful in, e.g., "a method of modulation of the catalytic activity of a protein kinase," the present claims recited that the method involves contacting said protein kinase with a compound, or salt or prodrug thereof of claim 1. Thus, the present method of use claims are of the same scope as

the product claims and as such should be rejoined according to the guidelines established pursuant to the decision in In re Ochiai.

Obviousness-Type Double Patenting

The Examiner has rejected claims 1-5, 9, 12, 15, 23 and 24 under the judicially created doctrine of obviousness type double patenting over the claims of U.S. Patent 6,395,734. Applicants respectfully traverse.

For a proper *prima facie* case of obviousness, three basic criteria must be met. This criteria applies to rejections based on 35 U.S.C. § 103 as well as obviousness type double patenting. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. In the case of obviousness-type double patenting, there must be some overlap of the claimed subject matter or the claimed subject matter must be an obvious variant compared to the claims of the patent. Second, there must be a reasonable expectation of success. Finally, the prior art references (or references when combined) must teach or suggest all the claim limitations. In obviousness-type double patenting rejections, the claims of the prior patent must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and **not based on applicant's disclosure**. See MPEP 2142.

In the case of an obviousness type double patenting rejection, the prior U.S. Patent claims must disclose or suggest each and every element of the claimed invention and there must be some reason to modify the claims of the patent to arrive at the claimed invention of the application. In the present case, the claims of U.S. Patent No. 6,395,734 fail to specifically teach or suggest that R⁹ is alkyl substituted with substituted or unsubstituted nitrogen, which the Examiner indicates is the "generic concept" identified for examination. The Examiner states in the Election/Restriction that the remaining subject matter stands withdrawn. Even though the claims, as originally presented, are generic to the claims of U.S. Patent No. 6,395,734, the subject matter that the Examiner has indicated as being examined is neither taught nor suggested by the patent claims of U.S. Patent No. 6,395,734. The Examiner's statement is true that the claimed subject matter is disclosed (but not claimed) in

U.S. Patent No. 6,395,734. That is because U.S. Patent No. 6,395,734 is the parent application to the present application. It is respectfully submitted there must be some motivation to modify the patent claims of U.S. Patent No. 6,395,734 to arrive at the presently claimed invention. Here, it appears that the Examiner has gleaned knowledge regarding the R⁹ moiety of alkyl substituted with substituted or unsubstituted nitrogen from Applicants own specification to arrive at the conclusion that the present claims are obvious over the claims of U.S. Patent No. 6,395,734. This is not a proper basis for a rejection based on obviousness-type double patenting. In the present case, such motivation is not present, thus, claims 1-23 of U.S. Patent No. 6,395,734 fail to teach all the claim limitations of the present claims.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested. In the alternative, the filing of a terminal disclaimer is held in abeyance until such time as the subject claims are in condition for allowance.

III. CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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By Mary C. Till

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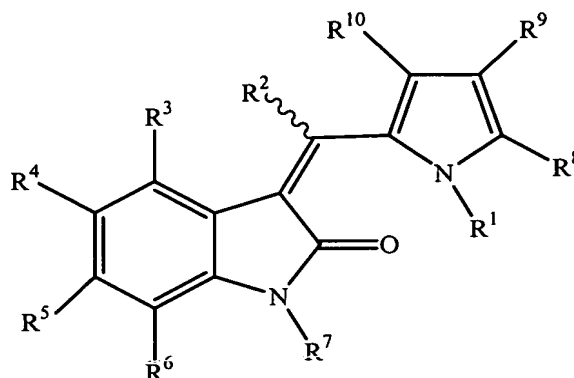
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A pyrrole substituted 2-indolinone having the chemical structure:



wherein

R^1 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, hydroxy, alkoxy, C-carboxy, O-carboxy, acetyl, C-amido, C-thioamido, sulfonyl and trihalomethanesulfonyl;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl and heterocyclic;

R^3 , R^4 , R^5 , and R^6 are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, sulfonyl, S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-carboxy, C-amido, N-amido, cyano, nitro, halo, O-carbamoyl, N-carbamoyl, O-thiocarbamoyl, N-thiocarbamoyl, amino and $-NR^{11}R^{12}$;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, carbonyl, acetyl, sulfonyl, trifluoromethanesulfonyl and, combined, a five- or six-member heteroalicyclic ring;

R^3 and R^4 , R^4 and R^5 , or [R^4 and R^5] R^5 and R^6 may combine to form a six-member aryl ring, a methylenedioxy group or an ethylenedioxy group;

R^7 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, carbonyl, acetyl, C-amido, C-thioamido, amidino, C-carboxy, O-carboxy, sulfonyl and trihalomethane-sulfonyl.

R^8 , R^9 and R^{10} are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, carbonyl, C-carboxy, O-carboxy, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino and $-NR^{11}R^{12}$, providing however that at least one of R^8 , R^9 and R^{10} is a group having the formula $-(alk_1)Z$;

R^9 is alkyl substituted with substituted or unsubstituted nitrogen;

Alk_1 is selected from the group consisting of alkyl, alkenyl and alkynyl; and,

Z is a polar group.

4. (Amended) The compound of claim 1 wherein R^3 , R^4 , R^5 and R^6 are independently selected from the group consisting of:

hydrogen;

halo;

unsubstituted lower alkyl;

lower alkyl substituted with one or more groups selected from the group consisting of:

hydroxy;

halo;

C-carboxy substituted with a group selected from the group consisting of:

hydrogen; or,

unsubstituted lower alkyl;

amino; or,

$-NR^{11}R^{12}$;

unsubstituted lower alkyl alkoxy;

lower alkyl alkoxy substituted with one or more halo groups;

unsubstituted aryloxy;

aryloxy substituted with one or more groups independently selected from the group consisting of:

unsubstituted lower alkyl;

lower alkyl substituted with one or more halo groups;

hydroxy;

unsubstituted lower alkyl alkoxy;

halo;
amino; or,
-NR¹¹R¹²;

S-sulfonamido wherein R¹¹ and R¹² are independently selected from the group consisting of
hydrogen and unsubstituted lower alkyl;

unsubstituted aryl;

aryl substituted with one or more groups independently selected from the group consisting of:

halo;
unsubstituted lower alkyl;
lower alkyl substituted with one or more halo groups;
unsubstituted lower alkyl alkoxy;
amino; or,
-NR¹¹R¹²;

unsubstituted heteroaryl;

heteroaryl substituted with one or more groups independently selected from the group
consisting of:

unsubstituted lower alkyl;
lower alkyl substituted with one or more halo groups;
unsubstituted lower alkyl alkoxy;
hydroxy;
halo;
amino; or,
-NR¹¹R¹²;

unsubstituted heteroalicyclic;

heteroalicyclic substituted with one or more groups independently selected from the group
consisting of:

halo;
hydroxy;
unsubstituted lower alkyl;
lower alkyl substituted with one or more halo groups;
unsubstituted lower alkyl alkoxy;

amino; or,

$[R^{11}R^{12};] -NR^{11}R^{12};$

unsubstituted lower alkyl O-carboxy;

C-amido wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen, unsubstituted lower alkyl and unsubstituted aryl; and,

N-amido wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen, unsubstituted lower alkyl and unsubstituted aryl.

5. (Amended) The compound of claim 3 wherein [wherein] R^3 , R^4 , R^5 and R^6 are selected from the group consisting of:

hydrogen;

halo;

unsubstituted lower alkyl;

lower alkyl substituted with one or more groups selected from the group consisting of:

hydroxy;

halo;

C-carboxy substituted with a group selected from the group consisting of:

hydrogen; or,

unsubstituted lower alkyl;

amino; or,

$-NR^{11}R^{12};$

unsubstituted lower alkyl alkoxy;

lower alkyl alkoxy substituted with one or more halo groups;

unsubstituted aryloxy;

aryloxy substituted with one or more groups independently selected from the group consisting of:

unsubstituted lower alkyl;

lower alkyl substituted with one or more halo groups;

hydroxy;

unsubstituted lower alkyl alkoxy;

halo;

amino; or,

-NR¹¹R¹²;

S-sulfonamido wherein R¹¹ and R¹² are independently selected from the group consisting of hydrogen and unsubstituted lower alkyl;

unsubstituted aryl;

aryl substituted with one or more groups independently selected from the group consisting of:

halo;

unsubstituted lower alkyl;

lower alkyl substituted with one or more halo groups;

unsubstituted lower alkyl alkoxy;

amino; or,

-NR¹¹R¹²;

unsubstituted heteroaryl;

heteroaryl substituted with one or more groups independently selected from the group consisting of:

unsubstituted lower alkyl;

lower alkyl substituted with one or more halo groups;

unsubstituted lower alkyl alkoxy;

hydroxy;

halo;

amino; or,

-NR¹¹R¹²;

unsubstituted heteroalicyclic;

heteroalicyclic substituted with one or more groups independently selected from the group consisting of:

halo;

hydroxy;

unsubstituted lower alkyl;

lower alkyl substituted with one or more halo groups;

unsubstituted lower alkyl alkoxy;

amino; or,

$[R^{11}R^{12};] \text{ -NR}^{11}R^{12}$.

unsubstituted lower alkyl O-carboxy;

C-amido wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen, unsubstituted lower alkyl and unsubstituted aryl; and,

N-amido wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen, unsubstituted lower alkyl and unsubstituted aryl.